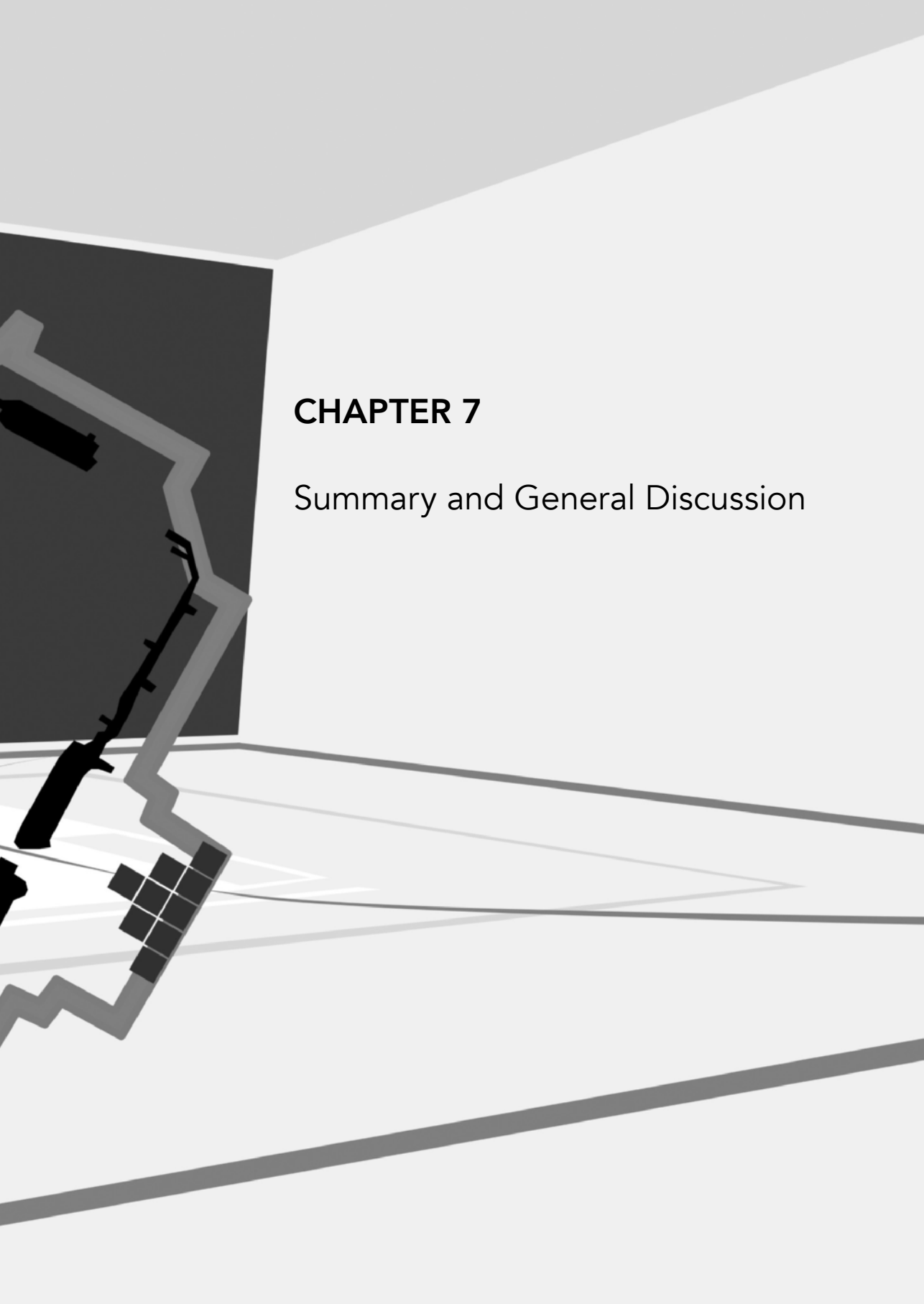
Treatment of antisocial behavior in adolescents

Jambroes, T.

2018

document version
Publisher's PDF, also known as Version of record



CHAPTER 7

Summary and General Discussion

SUMMARY

Juveniles who display antisocial behavior are at risk of unfavorable results with respect to their psychiatric, social and general functioning later in life (Abram et al., 2009; Abram et al., 2015; Knapp et al., 2011). However, even for some adolescents the most thorough interventions proved not to be effective, resulting in the persistence of antisocial behavior and delinquency (Boendermaker et al., 2013; Dam et al., 2010; De Swart et al., 2012). Consequently, an extensive body of research has focused on factors that relate to the persistence of antisocial behavior and negatively influence treatment effect. Based on research in psychopathic adults, the concept of the dimensions of psychopathy and antisocial behavior in children and adolescents has been studied to increase the understanding of persistent antisocial behavior in youth (Edens, Skeem, Cruise, & Cauffman, 2001; Frick, 2000). The affective features, also known as callous-unemotional dimension, showed to be related to a variety of negative outcomes (Frick et al., 2014b). Callous-Unemotional (CU)-traits typically reflect a lack of empathy and guilt, shallow emotions and callousness. CU-traits were linked to a severe, violent and persistent pattern of antisocial behavior and delinquent adolescents (Frick et al., 2014b). They showed to be relatively stable over time (Loney et al., 2007; Obradovic et al., 2007), and to negatively affect treatment outcome (Frick et al., 2014b). Although the current research findings on the association between CU-traits and persistent antisocial behavior in adolescents are convincing, questions remain regarding the role of CU-traits in predicting clinical improvement. Moreover, the potential role of other factors that additionally influence mechanisms of antisocial behavior in these adolescents needs to be elaborated. In this respect, there are indications for an interplay between neurobiological parameters and psychosocial risk factors in relation to persistent antisocial behavior (Van Goozen et al., 2007). One factor that is hypothesized to interact with specifically CU-traits is the low activity of the hypothalamic-pituitary-adrenal (HPA)-axis, the main endocrine stress regulatory system. Low arousal theories suggest that antisocial behavior is a result of an adverse physiological state. The sensation seeking theory states that subjects with a low arousal level will try to increase the arousal level to a normal state by displaying sensation seeking behavior, of which antisocial behavior can be seen as an extreme form (Zuckerman & Neeb, 1979). Alternatively, the fearlessness theory states that subjects with low arousal levels may not fear the negative

consequences of their behavior, and therefore do not keep away from antisocial behavior (Raine, 1993). It is suggested that specifically fearlessness, which is also characteristic for adolescents with CU-traits, may lead to a decreased responsiveness to interventions (Dadds & Rhodes, 2008; Stadler et al., 2010). Moreover, the relation between CU-traits and low arousal levels has been demonstrated in cross-sectional analysis (Burke et al., 2007; Stadler et al., 2011; Von Polier et al., 2013), though it was never tested in relation to treatment outcome. Thus, the aim of this study was to investigate whether CU-traits indeed relate to the severity of antisocial behaviour and decreased responsiveness to treatment. Secondly, it was studied whether low HPA-axis activity interacts with CU-traits in predicting treatment outcome. Five studies were conducted for the purpose of this thesis. The specific aims and results are summarized, followed by a general discussion.

All studies in this thesis were part of a large prospective longitudinal research project, focusing on adolescents in a closed treatment setting for youth with antisocial behavior. Adolescents are sent to this compulsory treatment by means of civil law court measures. They show severe antisocial behavior and seem unresponsive to generally used interventions (McCart et al., 2006). The most intensive forms of treatment are often provided in closed treatment settings. Closed placement is usually ordered by either civil or criminal law measures and is seen as a final opportunity to intervene. In the present study, the adolescents participating in a group intervention to reduce antisocial behavior were assessed at three time points during their stay in the facility: before and after the intervention, and before leaving the institution. During the assessments, saliva samples were collected to measure the cortisol levels, the hormonal end product of HPA-axis. CU-traits and the level of anti-social behavior were assessed by questionnaires that were filled out by both the participants themselves as well as group workers from the facility.

The aim of the study presented in **chapter 2** was to examine the relationships between dimensions of psychopathy and proactive and reactive aggression, and the moderating effect of verbal and performance intelligence. Previous studies clearly showed a relation between high levels of CU-traits and the severity of various forms of antisocial behavior (Frick et al., 2014b). However, other studies also underlined the relevance of the two other dimensions of psychopathy. Moreover, questions remain regarding the possible role of interacting factors on the relation between the dimensions of psychopathy and severity of anti-social

behavior, such as intelligence. Although some scholars did show an interactive effect between psychopathy, intelligence and anti-social behavior, they did not use a dimensional approach for all variables. Consequently, these findings need to be replicated to assess the moderating role of both verbal and performance intelligence on the relationship between dimensions of psychopathy and various forms of antisocial behavior. In our study, data regarding the dimensions of psychopathy and, proactive and reactive aggression were collected from the baseline diagnostic assessments. Intelligence rates were derived from the medical files of each participant. Regression analysis was performed and verified by an alternative, data driven generative discovery analysis. Results showed that the CU-dimension was positively related to proactive aggression, while reactive aggression was positively related to both the CU and II-dimensions. Moreover, verbal intelligence appeared to moderate these relations. In adolescents with high verbal intelligence scores, the CU-dimension showed a stronger positive relationship with proactive aggression, while adolescents with low verbal intelligence scores demonstrated a stronger positive relationship between the II-dimension and both reactive and proactive aggression. This study emphasizes the relevance of intelligence in defining the relation between dimensions of psychopathy and different forms of aggression. Moreover, CU-traits were specifically related with proactive aggression, which is considered to be the most severe and form of aggression.

A compelling question that comes up when subtyping youth with severe and persistent antisocial behavior based on CU-traits is whether pretreatment CU-traits negatively influence the outcome of an intervention. Review studies up until now could not draw firm conclusions, mainly because of the large variety in study characteristics between the single studies conducted (Frick et al., 2014b; Hawes et al., 2014; Waller et al., 2013; Wilkinson et al., 2016). Consequently, this called for a meta-analytic design, taking into account the variety in study characteristics. The meta-analytic systematic review study presented in **chapter 3** investigated whether pretreatment CU-traits affect treatment outcome in children and adolescents with antisocial behavior. Moreover, it was examined to which extent several study characteristics (sample, CU-assessment, treatment and outcome) moderated the relation between pretreatment CU-traits and treatment outcome. Overall, interventions showed a medium effect size on the clinical outcome measures. CU-traits did not moderate the effect of interventions directly. However, there were several characteristics that

interacted with CU-traits in its relation with effect sizes. Studies with smaller sample sizes and participants in a *treatment as usual* condition had a stronger relation between high CU-traits and a better treatment outcome than in studies with larger sample sizes or participants in the experimental condition. Likewise, when teachers reported on the CU traits, high CU-traits resulted in a greater reduction of antisocial behavior. There was no difference between the presence or absence of a systemic intervention, in both conditions high CU-traits resulted in worse treatment outcome. Finally, with respect to the antisocial behavior targeted by the intervention, high CU-traits resulted in less treatment effect when oppositional behavior was considered, while CU-traits related with better treatment outcome if delinquency was analyzed. Although this study shows a few characteristics that moderate the relation between CU-traits and treatment outcome, the main finding is that generally high levels of CU-traits do not relate with worse treatment outcome. This contradicts the believe that children and adolescents with severe and persistent antisocial behavior are resistant to change and encourages clinicians to include all youngsters, also those with high CU-traits in their treatment program.

HPA-axis activity

Over the last decades, research on neurobiological parameters aimed to increase the knowledge of mechanisms of antisocial behavior. Several studies demonstrated that the development and persistence of antisocial behavior in juveniles is influenced by neurobiological mechanisms (Van Goozen et al., 2007). Moreover, it is advocated that the interplay between neurobiological mechanisms and psychosocial risk factors specifically is relevant in understanding anti-social behavior, and may even help to identify adolescents with persistent antisocial behavior and poor treatment outcome (Van Goozen & Fairchild, 2008). In this respect, CU-traits and HPA-axis activity have been related with antisocial behavior and reduced treatment outcome. Consequently, their interplay may affect adolescents response to an intervention. This hypothesis is studied in **chapter 4**, by testing the relationship between pretreatment CU-traits and HPA-axis activity, and their interaction, with change in antisocial behavior during an intervention. All subjects participated in a standardized intervention aimed at reducing antisocial behavior, which was operationalized by a questionnaire measuring externalizing behavior. When considering single predictors, only the basal HPA-axis activity predicted change in externalizing problems. Increased

levels of HPA-axis activity at pretreatment were related to higher levels of externalizing problems during the intervention. Pretreatment CU-traits on its own did not predict an alteration in externalizing behavior, however, in interaction with the HPA-axis activity they did. In adolescents with high CU-traits, low HPA-axis reactivity was related to a decrease in externalizing problems, while high HPA-axis reactivity was related to an increase in externalizing behavior during the intervention. Remarkebly, low CU-traits, whether or not in combination with the HPA-axis reactivity, seemed to be less important in the prediction of treatment effect than adolescents with high CU-traits. This study suggests that HPA-axis dysregulation, especially in combination with high CU-traits, shows a unique association with treatment effect and indicates the relevance of integrating clinical and neurobiological factors to predict treatment effect.

The relation between CU-traits and HPA-axis activity over a longer period of time has not been investigated yet; all previous research used either cross-sectional approaches or only investigated the predictive value of pretreatment measures for treatment outcome. However, the relation between changes in CU-traits and HPA-axis functioning during an intervention may reveal important underlying neurobiological mechanisms in phenotypic changes due to interventions (Dadds & Rhodes, 2008; Hawes et al., 2009; Stadler et al., 2010). Therefore, the aim of the study presented in **chapter 5** was first to identify subgroups of adolescents based on their course of CU-traits during treatment. Then it was investigated whether the CU-subgroups differed in their development of HPA-axis activity. Participants were adolescents from a closed treatment institution that followed an intervention to reduce antisocial behavior. Assessments were conducted before and after the intervention, and at dismissal from the facility. CU-traits were measured with the Youth Psychopathic Traits-Inventory (YPI) and HPA-axis activity with the cortisol awakening response (CAR). Latent class analysis provided two subgroups of adolescents with different courses of CU-traits; one subgroup showed stable low CU-traits, and the other stable high CU-traits. For the total sample, HPA-axis activity did not differ between the CU-groups. However, for participants completing treatment and all cortisol-assessments, the HPA-axis activity in the high CU-group increased, reaching similar levels of HPA-axis activity as in the low CU-group. Based on these findings it appears that neurobiological changes in adolescents with antisocial behavior may occur during an intervention, whereas important phenotypical characteristics associated with persistent antisocial behavior remain stable.

A promising impulse for the use of CU-traits in clinical practice is the addition of the CU-traits related Limited Prosocial Emotions (LPE)-specifier in the classification of Conduct Disorder (CD) diagnosis in DSM 5. Although research indicates that the LPE specifier could identify a more severe antisocial subgroup within CD (Frick & Moffitt, 2010), knowledge on the relevance for clinical practice is scant. The study described in **chapter 6** aimed to test the clinical relevance of the new CU-traits related Limited Prosocial Emotions (LPE)-specifier in the classification of Conduct Disorder (CD) diagnosis of the DSM 5. It is argued that distinct subgroups of CD exist based on their developmental trajectory, and lead to different expressions of proactive and reactive aggression, rule breaking behavior and the absence or presence of internalizing problems. Subgroups of CD can be identified based on the age-of-onset (AoO) specifier in combination with the newly added LPE-specifier. Differences in behaviors of interest between subgroups of CD were analyzed. Subsequently, it was investigated whether the LPE specifier explains unique variance in aggression. The diagnosis of CD was obtained with a structured diagnostic interview (DISC). The LPE-specifier was based on the Youth Psychopathy Inventory (Colins & Andershed, 2014; Colins & Vermeiren, 2013). Aggression, rule-breaking behavior and internalizing problems were measured with questionnaires at the baseline assessment. The LPE-specifier, together with the AoO-specifier, revealed a difference in proactive and reactive aggression between mutually exclusive CD subgroups. Furthermore, the LPE specifier had some added predictive value for aggressive behavior, besides the single use of the AoO-specifier. It thus supports the implementation of the LPE specifier in the DSM 5. However, its additive value to assign clinical symptoms to CD proved small.

GENERAL DISCUSSION

The main aim of the studies presented in this thesis was to improve current knowledge of underlying mechanisms of reduced treatment outcome in adolescents with antisocial behavior. In a sample of adolescents in a closed treatment setting we focused specifically on the relevance of CU-traits during treatment. A major strength of this thesis is the integration of CU-traits with HPA-axis activity to test the interplay between a psychosocial risk factor and a neurobiological mechanism during an intervention. Herewith, we provided new insights in factors that relate to treatment outcome in adolescents with antisocial

behavior. However, we also demonstrated that the scientific knowledge on CU-traits should be translated to clinical practice with some reserve.

CU-traits and antisocial behavior

The results of the studies described in this thesis generally corroborate the prevailing idea that high CU-traits indicate a more severe subgroup of youth with antisocial behavior. First, our results show that, within the larger concept of psychopathy, it is specifically the high CU-traits dimension that is uniquely related to a more severe form of antisocial behavior, i.e. proactive aggression. Moreover, this relation is even stronger in adolescents with high verbal intelligence. In contrast, the II-dimension of psychopathy is related to both reactive aggression and proactive aggression, while these relations become stronger with lower verbal intelligence. In addition, the relevance of CU-traits in understanding antisocial behavior also show up in our subsample of adolescents that participated in the intervention to reduce antisocial behavior. Those adolescents with high CU-traits show the most externalizing behavior at pretreatment.

Second, our findings mostly confirm the relevance of the newly added CU-traits related LPE-specifier for conduct disorder criteria of the DSM 5. Adolescents with early onset CD and the LPE-specifier show more proactive and reactive aggression than those with late onset CD without the LPE-specifier. Although this result was only observed in combination with the age-of-onset specifier, it is in line with the aim of the LPE-specifier in the DSM 5: to designate a subgroup of youth with CD with severe antisocial behavior (Frick & Viding, 2009; Frick & White, 2008).

Finally, based on the course of CU-traits during an intervention, a stable high and a stable low CU-group were identified. Prior research has already shown the stability of elevated CU-traits across childhood and adolescence into adulthood (Burke et al., 2007; Munoz & Frick, 2007). These studies were mainly performed in young children in community settings with follow-up periods of several years to identify differences in normal development (Fanti et al., 2016; Fontaine et al., 2010; Klingzell et al., 2016). One specific study examined distinct courses of CU-traits during and shortly after a parent training intervention for young children, and reported a stable high, stable low and decreasing CU-trajectory subgroup (Hawes & Dadds, 2007). The results of the present thesis adds to previous findings that distinct courses of CU-traits can also be identified within a group of adolescents with severe behavioral problems following an intervention

in a closed treatment setting. This is an important finding, as it indicates that even within the group of adolescents with severe forms of antisocial behavior, such as those in closed treatment settings, subgroups can be identified based on the course of CU-traits. This implies that CU-traits can identify a subgroup which is thought to persist in its antisocial behavior. Contrary to other findings (Blader et al., 2013; Muratori et al., 2017), we did not identified a group with decreasing levels of CU-traits. Our sample contains adolescents with severe antisocial behavior, which most of them already exhibited for many years, without improving on the treatment offered. Consequently, it is plausible that specifically these adolescents with stable high CU-traits which are not sensitive to change, are overrepresented in closed treatment settings.

In conclusion, our results corroborate the knowledge that CU-traits relate with severe antisocial behavior, even in adolescents that are known to have serious conduct problems and are referred to a closed treatment institution. As such, they can be useful as a clinical feature in the assessment of adolescents with antisocial behavior. Specifically when used together with the age-of-onset specifier, they may improve the identification of distinct subgroups of adolescents. Moreover, in a subgroup of adolescents, CU-traits showed to be stable during their stay in the facility. This is a relevant finding as it can make clinicians more aware of a subgroup which may be more difficult to treat.

CU-traits related to treatment effect

Although the prevailing idea is that pretreatment CU-traits are predictive for a unfavorable treatment outcome, this thesis cannot confirm this. By structurally defining several characteristics of previous studies we were able to perform a multilevel meta-analysis on the influence of CU traits on treatment outcome, taking into account several relevant study characteristics. The main results show that CU-traits do not directly relate to treatment outcome. This finding was corroborated by the results of the longitudinal study in this thesis. In the adolescents that followed a group intervention to reduce antisocial behavior, pretreatment CU-traits did not relate with any alteration in antisocial behavior. However, our meta-analytic findings show that specific characteristics do influence the relation between CU-traits and treatment outcome. In this respect, the relation between CU-traits and treatment outcome differed depending on the informant that assesses the CU-traits. When teachers assess the CU-traits, treatment outcome was better in youth with high CU-traits while with parent

or self-reported CU-traits, treatment outcome was not related with the level of CU-traits. The finding that high CU-traits relate with better treatment outcome contrast with most other findings (Frick et al., 2014b; Hawes et al., 2014; Waller, Shaw, Forbes, & Hyde, 2015; Wilkinson et al., 2016). However, few studies showed similar results (Dadds et al., 2012; White et al., 2013). It is possible that individuals with high CU-traits also show the highest level of antisocial behavior at pretreatment and can, consequently, reach the biggest decrease due to the intervention. However, Dadds et al. (2012) showed that with a specific tailored intervention focusing on emotion recognition, youth with high CU-traits showed more improvements in affective empathy and conduct problems than those with low CU-traits. This emphasizes the need to further examine interventions that focus on this aspect. Moreover, as empathy impairments are hypothesized to play a central role in the development of CU-traits (Blair, 2008), treatment programs targeting those deficits may even have an important preventive effect in the development of antisocial behavior.

Thus, some previous research showed positive outcomes in treating youth with high CU-traits. However, to appreciate the association between CU-traits and treatment outcome, our thesis shows the necessity to account for the informant who assigns the CU-traits. In teachers reported CU-traits, treatment outcome was better, as opposed to parent-report or self-report of CU-traits. This informant difference in assigned CU-traits has been previously described, for instance in a validation study of two frequently used CU-questionnaires; the Antisocial Process Screening Device (APSD) and the Childhood Psychopathy Scale (CPS; Bijttebier & Decoene, 2009). It is argued that youth with conduct problems probably underestimate their behavior, and may therefore be less useful informants on these problems (Rolf Loeber et al., 1991). Likewise, it can be argued that parents underreport the CU-level as CU-traits are generally not socially desirable, whereas motivation for overreporting such behaviors appears less likely (Frick & Hare, 2001). To overcome these problems it is recommanded to merge ratings of multiple-informants to obtain a composite score (Piacentini et al., 1992). Although for several CU-questionnaires a multiple-informant method is possible (Bijttebier & Decoene, 2009; Dadds et al., 2005; Frick & Hare, 2001), very few studies that examined the relation between pretreatment CU-traits and treatment outcome used a composite score. This thesis shows the need to make use of multiple informants to increase the validation of CU-traits and

consequently the interpretation of studies testing their association with treatment outcome.

Further, the findings of the meta-analysis show the relevance of the outcome measure used. In youth with high CU-traits the treatment outcome is limited with regards to oppositional behavior. However, the treatment outcome in youth with high CU-traits is favorable when delinquent behavior is considered. This result is an important finding, as delinquency is one of the most worrisome behaviors and causes great distress in society. Our results show that such behavior is sensitive to change during an intervention, specifically in youth which were previously considered to be the most resistant to change and persisted in severe antisocial behavior, which are those youth with high CU-traits.

CU-traits combined with HPA-axis activity

In our thesis we integrate CU-traits and HPA-axis activity to test whether their interplay is relevant in the treatment effect of antisocial behavior in adolescents. Although their interplay has been shown in cross sectional analysis (Burke et al., 2007; Stadler et al., 2011; Von Polier et al., 2013), we addressed their interplay within a longitudinal design. In line with the low arousal theory, the results show that at pretreatment CU-traits interact with HPA-axis activity such that high CU-traits and decreased HPA-axis activity relate with the highest levels of antisocial behavior. As for treatment response, adolescents with high CU-traits in combination with low levels of arousal predicted a favorable treatment outcome; whereas high CU-traits with high levels of arousal predicted a worse treatment outcome. The results demonstrate that CU-traits have a unique interference with HPA-axis activity when related to treatment effect. Specifically in the high CU-traits, HPA-axis activity seems to interact in their prediction of treatment outcome. However, the direction of the interplay was contrary to what was expected according to the low arousal theory. Nevertheless, our findings lines up with others, arguing that high cortisol levels combined with daily stress may cause a replete HPA-axis system, leaving little capacity for therapeutic interventions (Schechter et al., 2012). As the current study was performed in a setting with severe and frequent daily stress, it may specifically have led to a reduced treatment effect in those adolescents with elevated levels of HPA-axis functioning. Additionally, it is shown that acute stress relates with increased activity of the HPA-axis, while chronic or frequent stress may lead to a sensitization of the HPA-axis (Ulrich-Lai & Herman, 2009). In the case of chronic stress, negative feedback mechanisms are thought

to cause a shift of internal set-point levels, which can be expressed by a reduced physiological function at rest and hyperreactivity to stressful situations (Ulrich-Lai & Herman, 2009). As adolescents in closed treatment settings have frequently experienced multiple trauma in their earlier lives (Ford et al., 2012; Hamerlynck et al., 2008), and the occurrence of daily stress events in these settings is high, the participants within this study may have had shifted HPA-axis functioning. Although the exact mechanisms remain unclear and should be studied in more detail, present results indicate that in adolescents with high CU-traits specifically, the integration of HPA-axis activity can enhance the prediction of treatment outcome. Consequently, this thesis reveals the potential value of integrating clinical and neurobiological factors to understand mechanisms that relate with persistent antisocial behavior and reduced treatment response.

This thesis further unravels the relation between CU-traits and HPA-axis activity in more detail by studying their longitudinal relation during treatment. First, a stable low CU-traits group and a stable high CU-traits group of adolescents could be identified. At pretreatment, the stable high CU-group showed lower HPA-axis activity than the stable low CU-group. This was expected according to the low arousal theory. However, after the intervention the HPA-axis activity in the high CU-group raised to similar levels as in the low CU-group. This finding is remarkable, as it was expected that HPA-axis activity in the stable high CU-group would remain low. Although previous research has shown that HPA-axis activity may increase during an intervention (Dorn et al., 2011; Motamedi et al., 2008; Nickel et al., 2006), this was not yet related to the course of CU-traits. Based on our findings it appears that neurobiological changes in adolescents with antisocial behavior may occur during an intervention, whereas CU-traits as an important phenotypical characteristic that is associated with persistent antisocial behavior remain stable. Our results resemble previous findings in foster children receiving multidimensional treatment foster care, who improved in their electrophysiological responses while their related behavioral measures showed no alterations (Bruce et al., 2009). Based on these findings, it could be speculated that a normalization of underlying neurobiological characteristics during an intervention may take place prior to a change in phenotypic features. However, our finding may also indicate that the neurobiological changes are indicative for alterations in clinical characteristics which are not accounted for in our study, such as fearlessness, aggression or other behavioral symptoms.

The results of our studies extended knowledge on mechanisms of severe and persistent antisocial behavior in adolescents. We outlined the relevance of CU-traits in combination with neurobiological characteristics, in identifying a severe subgroup of adolescents with antisocial behavior, and their influence on responsiveness to treatment. We demonstrated that CU-traits represent important clinical characteristics to determine a subgroup of adolescents with more severe antisocial behavior, even in adolescents admitted to a closed treatment facility. Although CU-traits were associated with severe forms of antisocial behavior, our studies also emphasize that other factors need to be accounted for in understanding antisocial behavior and reduced treatment response. This thesis showed the relevance of intelligence, the age of onset of conduct problems, and other dimensions of psychopathy. Moreover, this thesis specifically encourages to integrate neurobiological measures with clinical characteristics, as this may further increase our understanding of mechanisms of severe and persistent antisocial behavior and their response to treatment.

Strengths and limitations

There are some limitations of this thesis that should be considered when interpreting the results.

First, it must be considered that we studied a specific population of severely antisocial adolescents in a closed treatment setting. This means that the results cannot be generalized directly for other samples, such as children in a community setting. Our sample contains adolescents already showing high rates of antisocial behavior, as this is frequently the reason of sending them to such a setting. Therefore, the findings in our studies specifically reflect on this group and, as a consequence, we cannot generalize these findings to a normal population with significant less antisocial behavioral problems. Second, there was a considerable amount of participants lost for follow-up measurements. Although these numbers of missings can be expected in closed facilities and are comparable with other longitudinal research on HPA-axis activity in youth with conduct problems (Dorn et al., 2011), they have influenced the statistical strength. Nevertheless, we were able to extract several statistically significant and clinically relevant findings. However, as the sample was heterogeneous, we were restricted and could not look into more detailed subgroups. Third, our study was performed in adolescents with severe behavioral problems with drug and alcohol use, and traumatic life experiences. Studies have shown that alcohol and drug use at a

young age permanently impairs cognitive flexibility (Brown et al., 2008), and exposure to violence and traumatic life events in young people were associated with CU-traits (Howard, Kimonis, Muñoz, & Frick, 2012; Kahn et al., 2013; Kimonis, Frick, Munoz, & Aucoin, 2008). As these possible confounders were not accounted for in this study, they might have influenced the results. Forth, it must be considered that although all participants followed the same intervention to reduce antisocial behavior, it is not known whether participants received any additional treatment during their stay in the institution. As a result, it is possible that participants received additional effective interventions, which contributed to the alterations. Therefore, changes in antisocial behavior as measured in our studies should be seen as an effect of closed setting treatment overall and not as something solely caused by the intervention. Moreover, it should be noted that the aim of the study was not to establish the effect of treatment per se, but to assess differences between subgroups with different levels of CU traits. Finally, our results rely on the use of only one CU-traits questionnaire, filled in by the younth themselves. As shown in this thesis, the association between CU-traits and treatment outcome depends on who has administered the CU-traits questionnaire. Consequently, the results in this thesis must be considered in this light.

Clinical implications

Present findings have several implications for clinical practice. The findings show that within a closed treatment setting for adolescents with antisocial behavior, subgroups can be identified based on the level of CU-traits. Therefore, clinical assessment of CU-traits can help to understand behavior and thereby improve the diagnostics and treatment indications. To increase the validity of the assessment it is advised to make use of multiple informants in order to produce a composite CU-traits score. The assignment of interventions can subsequently be tailored to the individual needs. Verbal intelligence showed to affect the relation between CU-traits and specific types of antisocial behavior. As a result, this can help to improve intervention effectiveness by differentiating between the types of antisocial behavior involved. Further, the intelligence level can help to choose which intervention is preferred. In adolescents with low intelligence and reactive aggression, behavioral therapy or pharmacological treatment targeting impulsive behavior should be advised, as these interventions depend less on verbal abilities. For the treatment of proactive aggressive behavior in adolescents

on the other hand, interventions that appeal to good verbal abilities can be used to improve the emotional recognition component of CU-traits.

Besides the measuring of CU-traits, our results give support to the incorporation of neurobiological measurements into the clinical practice of treating adolescents with antisocial behavior. Although the current knowledge is too limited to structurally use HPA-axis activity measurements in standardized treatment programs, they may be beneficial for personalized intervention (Beekman, van Amelsvoort, Van, & Goethals, 2018). The combined use of CU-traits and HPA-axis activity may improve the prediction of treatment outcome. Moreover, it can offer arguments to either stop or continue an intervention. Our results show that in adolescents with high CU-traits and low HPA-axis functioning, the reduction of antisocial behavior continues until they are dismissed from the facility. This presents arguments to prolong treatment for these individuals as they may continue to improve their behavior. However, it can also be debated whether this treatment needs to be applied in a closed treatment setting or whether an outpatient intervention can be equally, or even more, effective. This thesis cannot elucidate this question. Adolescents with high CU-traits and elevated HPA-axis activity, however, seem to be at risk for an increase in antisocial behavior during closed treatment. Clinicians should be aware of this. It can be argued that for these adolescents, assignment to a closed treatment setting can have an adverse effect. Disregarding societal safety aspects, these adolescents should be withheld from a closed placement and offered other type of interventions. Further, clinicians treating adolescents displaying antisocial behavior should start measuring HPA-axis activity levels during an intervention for the personalized evaluation of treatment response. Present results show that although CU-traits remained stable, HPA-axis activity changed during the intervention. This occured specifically in the group with stable high CU-traits, which are supposed to be the most difficult to treat and persist in antisocial behavior. Consequently, levels of HPA-axis activity can be an independent measure to inform clinicians whether the intervention leads to changes in characteristics that are related to mechanisms of antisocial behavior.

Finally, in order to identify a more severe subgroup in clinical practice, DSM 5 has added the LPE-specifier to the diagnosis of CD. The LPE-specifier delivers a dichotomous outcome, it is either present or not. However, based on our results, its additive value to assign clinical symptoms to CD proved to be small in an adolescent sample with antisocial behavior. In this respect, the clinical usefulness

of the specifier could be argued. An important drawback of the LPE-specifier is the dichotomous outcome, which makes it less useful in evaluating alterations during interventions. Besides proper DMS 5 classifications, it is therefore advised to make use of questionnaires that offer continuous values of CU-traits.

Future research

The current thesis has brought us a step forward in understanding mechanisms underlying antisocial behavior in adolescents by studying CU-traits and HPA-axis activity during treatment. This entails some practical implications for future research and issues that need to be investigated to further improve the integration of clinical and neurobiological factors.

Although our findings uncovered the usefulness of integrating CU-traits and HPA-axis activity to predict and evaluate treatment outcome, several issues need to be elaborated upon further. First, our results show that the way CU-traits are assessed is of great relevance for the understanding of their relation with antisocial behavior. However, to date there exists a variety of questionnaires to assess CU-traits, making use of various informants. Future studies should further test the incremental validity of CU-traits scores based on multiple informants, in stead of using single informant CU-traits scores in predicting treatment outcome. Likewise, it should be studied whether the LPE-specifier for CD disorder in the DSM 5 has a predictive value for treatment outcome of antisocial behavior.

Second, current findings encourage future studies to search for longitudinal trajectories of CU-traits and HPA-axis functioning during interventions, and link them with target symptoms such as fearlessness and aggression. These findings may lead to the structural measuring of HPA-axis activity during treatment as an assessment tool to evaluate treatment response. Interventions can thus be tailored to the specific needs of adolescents and result in better treatment outcome.

Finally, it is important to make use of various outcome measures to evaluate future interventions. As treatment programs for adolescents with antisocial behavior target several forms of antisocial behavior, it is necessary to evaluate treatment response on all these forms as well. This can further increase the knowledge of mechanisms of antisocial behavior during an intervention.